RESPONSE

I. Status of the Claims

Claim 2 has been cancelled without prejudice and without disclaimer. Claim 12 has been amended. New claims 16 and 17 have been added.

Claims 1, 3 and 11-17 are therefore presently pending in the case.

II. Support for the Amended and Newly Added Claims

Claim 12 has been amended to correct an inadvertent typographical error by inserting a period at the end of the claim.

Claims 16 and 17 have been added to specifically recite alternative embodiments of claim 15. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 15, and from page 15, line 33 to page 16, line 6.

It will be understood that no new matter is included within the amended or newly added claims.

III. Information Disclosure Statement

The Action next objects to the information disclosure statement ("IDS") filed on June 28, 2002, as allegedly failing to comply with the provisions of 37 C.F.R. § 1.98(a)(2), apparently because **none** of the **63** references submitted with the IDS can be located by the Examiner. The Examiner graciously admits that "(n)o fault is laid on the Applicant" (Action at page 2) for the failure of the United States Patent and Trademark Office ("USPTO") to properly handle the 63 references that were submitted by Applicants on June 28, 2002, and received by the USPTO on July 2, 2002, as evidenced by the postcard received by Applicants. The Examiner further "invites the Applicant to supply a replacement IDS accompanying the response to this Office Action at no charge" (Action at page 2). Since the USPTO is fully and totally responsible for "misplacing" the 63 references already provided by Applicants, Applicants are well aware that no fees under 37 C.F.R. 1.97(c) are due in connection with the filing of a "replacement IDS". Applicants do note for the record, however, that the filing of a "replacement IDS" DOES in fact have a **cost**, specifically, the **cost** of copying each of the 63 references, the **cost** of mailing the 63 references to the USPTO, not to mention the **cost** in time of having to perform each of these tasks, each of which costs are born by Applicants alone (and have been born by Applicants numerous times previously because of IDSs that have been "misplaced" by

the USPTO).

Nevertheless, Applicants have no alternative but to provide a "replacement IDS", and do so herewith. Applicants can only hope that the USPTO does not also "misplace" the "replacement IDS".

IV. Oath/Declaration

The Action next objects to the declaration as defective, as allegedly a non-initialed and/or non-dated alteration has been made to the oath or declaration. Applicants respectfully point out that 37 C.F.R. § 1.52(c)(1) requires "(a)ny interlineation, erasure, cancellation or other alteration ... should be dated and initialed or signed by the applicant on the same sheet of paper" (37 C.F.R. § 1.52(c)(1), emphasis added). As inventor Wilganowski did in fact sign and date the declaration containing the interlineated address "on the same sheet of paper" containing the correction, it is Applicants' position that the declaration filed on June 28, 2002, is in fact NOT defective. Applicants therefore believe that new declaration is not required in the present case.

However, should the Office provide evidence that Applicants' interpretation of 37 C.F.R. § 1.52(c)(1) is incorrect, Applicants will gladly provide a new declaration that is in compliance with 37 C.F.R. § 1.67(a).

V. Claim Objection

The Action objects to claim 12, since "claim 12 does not end in a period" (Action at page 3). Applicants apologize for the inadvertent typographical error, and have amended claim 12 to include a period at the end of the claim.

Applicants request that, since the objection has been overcome, this objection be withdrawn.

VI. Rejection of Claims 1-3 and 11-15 Under 35 U.S.C. § 101

The Action first rejects claims 1-3 and 11-15 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that claim 2 lacks a patentable utility, as claim 2 has been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claim 2 under 35 U.S.C. § 101 is rendered moot. The remainder of this section will therefore focus on claims 1, 3 and 11-15.

In the Action, the Examiner questions Applicants' assertion that the present sequence has a patentable utility as a sodium/bile co-transporter. Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55; **Exhibit A**) clearly establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility (see Section VII, below), is not proper when a full length sequence (such as the presently claimed sequence) has a similarity score greater than 95% to a protein having a "well established utility". Applicants respectfully point out that the amino acid sequence encoded by the presently claimed nucleotide sequence shares **100% identity** at the amino acid level with a sequence that is present in the leading scientific repository for biological sequence data (GenBank), and which has been annotated by Prof. Dr. Ernst Petzinger, an independent third party scientist *wholly unaffiliated with Applicants*, who has numerous publications concerning organic anion transporters (**Exhibit B**), as Homo sapiens mRNA for sodium-dependent organic anion transporter (GenBank accession number AJ583502, alignment and GenBank report provided in **Exhibit C**). Furthermore, it is well-known in the art that bile is an example of an organic anion that is co-transported with sodium ion. The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art (such as Prof. Dr. Petzinger, would clearly believe that Applicants' sequence is a sodium/bile co-transporter, exactly as asserted by Applicants in the specification as originally filed (at least at page 2, lines 11-15), and therefore, would have numerous uses, including those detailed below. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner states that "(i)t is not clear from the specification ... what tissues are it (*sic*) expressed in" (Action at page 4). Applicants respectfully point out that the specification as originally filed clearly states that the presently claimed sequence is "expressed in, *inter alia,* human cell lines, brain, pituitary, spinal cord, thymus, spleen, lymph node, trachea, lung, kidney, prostate, testis, thyroid, adrenal gland, pancreas, salivary gland, stomach, small intestine, colon, skeletal muscle, heart, uterus, placenta, mammary gland, adipose, skin, esophagus, bladder, cervix, pericardium, fetal kidney, fetal lung, gall bladder, tongue, aorta, and 6-week old embryos" (page 4, lines 3-11). Thus, this argument does not support the Examiner's position that the presently claimed sequence lacks a patentable utility.

It has been well established that Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In*

re Gottlieb, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), and, thus, any questions concerning whether or not the present claims meet the requirements of 35 U.S.C. § 101 should have been laid to rest. Nevertheless, Applicants point out that the present invention has a number of other patentable utilities, for example the utility of tracking expression of the presently claimed sequence. The specification details, at least at page 6, lines 31-33, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of human chromosome 4 (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, *Science* **291**:1304, 2001). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny

and Kennedy, *Science* **291**:1153, 2001). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

While the Examiner states that "(t)his asserted utility is credible", he concludes that it "is neither substantial nor specific" because "there is no substantial utility for the encoded polypeptide" (Action at page 8). This argument has been dealt with above, in showing that those of skill in the art would readily believe that the presently claimed sequence encodes a sodium/bile co-transporter. Next, the Examiner states that "since all nucleic acids can be used as probes or primers, this asserted utility is not specific" (Action at page 8). This argument is flawed in at least two respects. First, Applicants respectfully point out that only expressed sequences can be used to track gene expression, not just any nucleic acid. Expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Skilled artisans already have used and continue to use sequences such as Applicants in gene chip applications without any further experimentation. Second, the Examiner seems to be confusing the requirements of a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with that of a **unique** utility, which is clearly an improper standard. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

The fact that other nucleotide sequences can be used to track gene expression does not mean that the use of Applicants' sequence to track gene expression is not a specific utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf;

and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

As yet a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 3, lines 11-14, the present nucleotide sequence has a specific utility in "identification of protein coding sequences" and "mapping a unique gene to a particular chromosome". As described in the specification as originally filed at page 18, lines 21-22, the gene encoding the presently claimed sequences is present on "human chromosome 4 (see GENBANK accession no. AC079237)". In fact, alignment of the presently claimed sequence with GenBank accession numbers AC079237 and AC105413 (two overlapping genomic clones from human chromosome 4) shows that the human gene corresponding to the presently claimed sequence is dispersed on 6 exons of human chromosome 4 (alignment and first pages of the GenBank reports are presented in **Exhibit D**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 4 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions this utility, first stating the "substantial further research would be

required for the skilled artisan to determine where this particular sequence is mapped in order to use the nucleic acid molecule in the asserted utility as a chromosomal map probe" (Action at page 12). Applicants respectfully point out that the standard for complying with 35 U.S.C. § 101 is not whether "further research" is required, but, rather, whether undue experimentation is required. Furthermore, in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Applicants point out that the skilled artisan can use the sequence information provided by Applicants, along with a standard computer system equipped with standard nucleic acid comparison software, many examples of which are well-known in the art, to conduct the exact same analysis performed by Applicants, the results of which are shown in **Exhibit D**, without undue experimentation. This is all that is required for the claims to meet the requirements of 35 U.S.C. § 101.

The Examiner then states that "the asserted utility is also not specific, since the entire class of genes can be asserted to be used in this way" (Action at page 13). First, Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). As described in the specification as originally filed at page 3, lines 14-17, the claimed sequences "identify biologically verified exon splice junctions, as opposed to splice junctions that may have been bioinformatically predicted from genomic sequence alone". The specification also details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification at page 12, lines 17-23). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. Second, the Examiner again seems to be confusing the requirements

of a **specific** utility with a **unique** utility. The fact that other nucleotide sequences can be used to identify exon splice junctions and map human chromosome 4 does not mean that these uses of Applicants' sequence are not specific utilities (*Carl Zeiss Stiftung v. Renishaw PLC, supra*). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Absent such evidence from the Examiner, as the skilled artisan would readily understand that the presently claimed sequence has a number of utilities, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

Furthermore, in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug

for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the presently claimed sequence has a number of utilities, without the need for any further research. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). Applicants reiterate that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra.* The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra.* As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.*

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for

compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VII, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-3 and 11-15 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

VII. Rejection of Claims 1-3 and 11-15 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3 and 11-15 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is

not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that one skilled in the art would not know how to use the invention as set forth in claim 2, since claim 2 has been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claim 2 under 35 U.S.C. § 112, first paragraph is rendered moot. The remainder of this section will therefore focus on claims 1, 3 and 11-15.

Applicants submit that as claims 1, 3 and 11-15 have been shown to have "a specific, substantial, and credible utility", as detailed in section VI above, the present rejection of claims 1, 3 and 11-15 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-3 and 11-15 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VIII. Rejection of Claims 1, 2, 12, 13 and 15 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1, 2, 12, 13 and 15 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 59 contiguous nucleotides of SEQ ID NO:1. Applicants respectfully traverse.

The Action admits that "(t)he specification teaches that SEQ ID NO:1 encodes SEQ ID NO:2", but that "the specification fails to provide any guidance for the successful characterization of SEQ ID NO:1's encoded polypeptide's function or any fragments thereof" (Action at page 15). Applicants point out that the above comment is completely irrelevant to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. Therefore, Applicants submit that the Examiner has failed to present reasoning sufficient to establish a *prima facie* case supporting the present § 112 rejection, and accordingly the rejection is improper because: 1) the Examiner's comments were not relevant to the established legal standard of enablement; 2) the Examiner's failure to attribute adequate weight and attention to the detailed level of teaching clearly provided in the specification; and 3) the reasoning for the enablement rejection provided by the Examiner failed to adequately consider the high level of technical knowledge that can be attributed to those skilled in the art in the field of the present invention.

A. Enablement is Established by Enabling Any Practical Use

In attempting to establish a *prima facie* case to support the § 112 rejection of the composition claims, the Action questions whether the claimed compositions are sufficiently enabled to allow those skilled in the art to practice aspects of the invention involving standard molecular biological techniques. The § 112 rejection, as applied against the nucleic acid compositions, is completely misplaced. It has long been established that composition claims are enabled by defining any practical use of the claimed compound. *In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka, supra.* "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991).

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed in Section VI, above, in *In re Brana, supra*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner states that the present invention could not be practiced without "undue trial and error experimentation" (Action at page 15). However, it is important to remember that, as discussed above in Section VI, in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra.* In *Wands, supra*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in

> order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra.*

The Action cites Wong *et al.* (*J. Biol. Chem.* **270**:27728 (*sic*; 27228)-27234, 1995), Wells (Biochemistry 29:8509-8517, 1990), Ngo *et al.* (*The Protein Folding Problem and Tertiary Structure Prediction*, Merz *et al.* (ed.) Birkhauser, Boston, MA, pp. 492-495, 1995), Bork (*Genome Research* **10**:398-400, 2000), Skolnick and Fetrow (*Trends in Biotech.* **18**:34-39, 2000), Doerks *et al.* (*Trends n Genetics* **14**:248-250, 1998), Smith and Zhang (*Nature Biotechnology* **15**:1222-1223, 1997), Brenner (*Trends in Genetics* **15**:1320133, 1999) and Bork and Bairoch (*Trends in Genetics* **12**:425-427, 1996) to support the proposition that the relationship between sequence of a protein and its activity is not well understood, based on the premise that small changes in amino acid sequence can lead to proteins having different functions. First, Applicants respectfully point out that the **PTO itself** does **not** require 100% identity between sequences to establish a functional relationship. Example 10 of the Revised Interim Utility Guidelines Training Materials (see **Exhibit A**) clearly establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility (see Section VI and VII, above), is not proper when a full length sequence (such as the presently claimed sequence) has a similarity score greater than **95%** to a protein having a known function. Thus, even if the Examiner's premise concerning functionality germane to the present rejection under 35 U.S.C. § 112, first paragraph, these references themselves, in addition to the numerous shortcomings of these references with regard to the specifically claimed sequence, would not support the Examiner's position.

However, second, and most importantly, the Examiner's argument concerning functionality is completely misplaced, because numerous uses of the claimed sequences do not require knowledge of **any** functional aspects of the amino acid sequences. Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short,

overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section VI, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

Even though the burden has been improperly shifted to Applicants, the following section is being provided to demonstrate that the specification is fully enabling in view of the detailed guidance and teaching provided in the specification within the context of the high level of technical knowledge present in the art regarding the use of nucleic acids such as those presently claimed..

B. The Specification Provides Adequate Guidance and Teaching

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought

> to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.* In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

C. Claims 1, 2, 12, 13 and 15 are Enabled

As detailed in the sections above, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

IX. Rejection of Claims 1, 12 and 15 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1, 12 and 15 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable

clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

The Examiner states that the written description requirement for a claimed genus may be satisfied through "disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, **and** any combination thereof" (Action bridging pages 19 and 20, emphasis added). Applicants respectfully point out that the Examiner has misquoted the PTO Guidelines (66 Fed. Reg. at 1106), replacing the werd "or" in the guidelines with the word "and", emphasized in the quote above. This is an extremely important distinction. In fact, in its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, **or** some combination of such characteristics" (66 Fed. Reg. at 1106, emphasis added). The Federal Circuit has recently confirmed this aspect of the PTO Guidelines, wherein this exact quote was reproduced (*Enzo Biochem, Inc. v. Gen-Probe, Inc. et al.* (296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)). Taking the exact statement from the PTO Guidelines clause by clause, the written description requirement for a claimed genus may be satisfied through disclosure of sufficiently detailed, relevant identifying characteristics, which are defined as: (a) complete or partial structure; (b) other physical and/or chemical properties; (c) functional characteristics when coupled with a known or disclosed correlation between function and structure; **or** (d) some combination of such characteristics. In other words, the written description requirement is satisfied by (a), (b), (c) **or** (d). Clause (a) states that the written description requirement may be satisfied by the disclosure of structure. The Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish

the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph. Thus, the present claims are in clearly in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides comprising at least 59 contiguous bases of nucleotide sequence first disclosed in SEQ ID NO:1 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claims 1, 12 and 15 thus meet the written description requirement.

Applicants therefore respectfully request that the rejection of claims 1, 12 and 15 under

35 U.S.C. § 112, first paragraph, be withdrawn.

X. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term "stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance, claim 2 has been cancelled without prejudice and without disclaimer, rendering the present rejection moot.

As the rejection of claim 2 under 35 U.S.C. § 112, second paragraph, has been rendered moot, Applicants respectfully request withdrawal of this rejection.

XI. Rejection of Claim 1 Under 35 U.S.C. § 102(b)

The Action next rejects claim 1 under 35 U.S.C. § 102(b), as allegedly anticipated by Sulston *et al.* (1998, *Genome Res.* **8**:1097, as allegedly exemplified by GenBank Database accession number AC079237; "Sulston"). Applicants respectfully traverse.

It is well-known that to qualify as prior art, a reference must be "patented or described in a printed publication in this or a foreign country ... more than one year prior to the date of the application for patent in the United States" (35 U.S.C. § 102(b), emphasis added). The Action states that Sulston "disclose a nucleic acid sequence which (*sic*) shares 100% sequence homology with bp 1-377 of SEQ ID NO:1" (Action at page 22). The Examiner appears to believe that the sequence presented in GenBank accession number AC079237 is disclosed in Sulston, because Sulston is listed as reference number 1 in the GenBank report for accession number AC079237. However, a careful review of Sulston reveals that not only is "a nucleic acid sequence which (*sic*) shares 100% sequence homology with bp 1-377 of SEQ ID NO:1" **not** disclosed, but in fact **no DNA sequence is disclosed**. Closer examination of the remaining portion of the GenBank report for AC079237 (see the first page of the GenBank report for AC079237 presented in **Exhibit D**), which was not provided by the Examiner

with the Action, indicates that reference number 2 is titled "The sequence of Homo sapiens BAC clone RP11-711J3", which in fact is the sequence disclosed in AC079237. Furthermore, this sequence is indicated as "Unpublished (2001)". Therefore, the 102(b) date of GenBank accession number AC079237 is controlling. The date that AC079237 was released to the public was February 21, 2002 (see **Exhibit D**). The present application, filed on March 6, 2002, properly claims the benefit of U.S. Provisional Application Numbers 60/275,009 and 60/284,152, which were filed on March 12, 2001 and April 17, 2001, respectively, over 10 months before the AC079237 sequence became publicly available. Thus, AC079237 is not properly used as prior art against the present application.

Additionally, Applicants point out that an allegation that Sulston inherently contains "a nucleic acid sequence which (*sic*) shares 100% sequence homology with bp 1-377 of SEQ ID NO:1" would fall far short of the level required to establish a *prima facie* case of anticipation. Importantly, there is **no mention at all** of *Homo sapiens* BAC clone RP11-711J3 in Sulston. Additionally, the mere listing of a reference in a GenBank report is not necessarily indicative, let alone dispositive, of whether the cited reference contains the sequence in question. Numerous GenBank reports contain references that are merely general in nature, and do not specifically contain the annotated sequence. As just one example, the GenBank report NM_008337 lists **101 references, all but one of which** are annotated as concerning bases 1-1208 of the mouse gamma interferon sequence (**Exhibit E**). Clearly, all 100 of these references do not report the 1,208 base pair mouse interferon gamma nucleotide sequence. Absent **evidence** that the authors of the Sulston reference had possession of the *Homo sapiens* BAC clone RP11-711J3 prior to Applicants' priority date, a *prima facie* case of anticipation cannot be established, and a rejection of claim 1 under 35 U.S.C. § 102(a) based on inherent anticipation could not be sustained.

Furthermore, the Federal Circuit has long held that the actual DNA sequence is necessary for anticipation. "We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). For Sulston to inherently anticipate the claimed nucleic acid sequence, there would need to be evidence that *Homo sapiens* BAC clone RP11-711J3 was in the possession of the authors of the Sulston reference at the time the Sulston reference was published, and further that the sequence presented in

GenBank accession number AC079237 was the sequence of the exact same *Homo sapiens* BAC clone RP11-711J3 isolate that was in the possession of the authors of the Sulston reference. Absent such evidence, which is clearly lacking in this case, a rejection of claim 1 under 35 U.S.C. § 102(a) based on inherent anticipation must fail.

While it is true that "[A] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference" *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), it has clearly been established that "[T]he identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). This "detail" is clearly lacking from the Sulston reference. Furthermore, the Federal Circuit has clearly established that "[A] claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." (*Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003)). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). As the skilled artisan could not practice the claimed invention, specifically an isolated nucleic acid molecule comprising at least 59 contiguous nucleotides from SEQ ID NO:1, using their own knowledge and Sulston alone, a *prima facie* case for anticipation cannot be established, and a rejection of claim 1 under 35 U.S.C. § 102(a) based on inherent anticipation must fail.

Additionally, even if, *arguendo*, a court were to find that a *prima facie* case for anticipation has been established, the showing required for inherent anticipation requires more than the possibility that "a nucleic acid sequence which (*sic*) shares 100% sequence homology with bp 1-377 of SEQ ID NO:1" is inherently contained in Sulston. The abstract of Sulston indicates that the authors "have identified the map position of bacterial clones covering ~860 Mb for sequencing and completed >98 Mb (~3.3%) of the human genome sequence". However, as discussed above, there is **no mention at all** of *Homo sapiens* BAC clone RP11-711J3 in Sulston. The mere possibility that one of the clones alluded to in Sulston is *Homo sapiens* BAC clone RP11-711J3 does not meet the burden required to show inherent anticipation. As clearly established by the Federal Circuit in *Mentor v. Medical Device Alliance* (244 F.3d 1365, 58 USPQ2d 1321 (Fed. Cir. 2001)), "(t)he

trial testimony does not meet the threshold for showing inherent anticipation, which may not be established by 'probabilities or possibilities.' *See MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999) (citing *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981)). The mere fact that a certain thing may result from a given set of circumstances is not sufficient" (emphasis in original). This is also confirmed by examination of the MPEP, Section 2112, which clearly states "[T]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic" (emphasis in original). In other words, the mere fact that the authors of the Sulston reference **may** have possessed the *Homo sapiens* BAC clone RP11-711J3 is not enough for a finding of inherent anticipation. Thus, the burden for establishing inherent anticipation cannot be met, and a rejection of claim 1 under 35 U.S.C. § 102(a) based on inherent anticipation must fail.

Therefore, as Sulston does not teach or suggest, directly or inherently, an isolated nucleic acid molecule comprising at least 59 contiguous nucleotides from SEQ ID NO:1, and AC079237 is not properly used as prior art against the present application, Applicants submit that the present rejection of claim 1 under 35 U.S.C. § 102(a) over Sulston is improper, and should be withdrawn.

XII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Nichols have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

February 9, 2004
Date

David W. Hibler Reg. No. 41,071
Agent for Applicants

CUSTOMER NUMBER
24231

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399